



PHILIP MORRIS

INCORPORATED

Law Department—Patent Section

RESEARCH CENTER: P.O. BOX 26583, RICHMOND, VIRGINIA 23261 TELEPHONE (804) 271-2000

19 December 1979

George A. Depaoli, Esq.
Depaoli & O'Brien
Suite 1005 Crystal Mall I
1911 Jefferson Davis Highway
Arlington VA 22202

RE: PROCESS FOR THE PREPARATION OF OPTICALLY ACTIVE
NICOTINE ANALOGUES/PM 883A/Chavdarian & Sanders/D&O-79-9

Dear George:

Enclosed is the corrected application for PM 883. Minor typographical errors in the application have been noted. A note is attached on page 4 of the application and suggested nomenclature changes are indicated. I don't know whether it is proper to change names in referenced articles so we shall rely on your judgement.

On page 9 and 10 two different compounds are shown as formula III. The formula on page 9 needs a new designation (II¹, IIa or something); otherwise, massive revision of all subsequent formula numbers would be necessary. I'm sure you want to avoid that if possible.

After carefully reading the claims, we feel they are very comprehensive and only require several minor revisions. There is some question in the inventors' minds regarding formula numbers. See specifically Claims 1 and 30. I think we are clear on Claim 27, however, you might take another look at it in view of Claim 4. See also Claims 36 and 41. It does not appear that enantiomerically pure 6-methylnicotine is embraced by either claim. If you feel this compound is patentable, then perhaps one or the other claim should be revised. See the Haglid reference at page 2 of the specification.

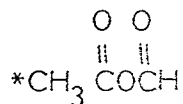
Regarding your question about the chemistry involved in the preparation of IVb [(-)-N-formylproline], Dr. Chavarian has stated that "the use of formic acid and acetic anhydride results in formation of the mixed anhydride, formyl acetate*, which is a good reagent for formylating amines. The formyl group of this mixed anhydride reacts in preference to the acetyl group."

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George A. Depaoli, Esq.

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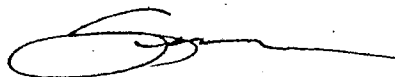


If you feel further discussion is necessary regarding any of the above points, please give me a call.

I hope to have some information on Sander's and Seeman's 883B case soon. As you know Dr. Seeman is on an extended vacation and will not return until about January 4.

****HAPPY HOLIDAY****

Very truly yours,



Susan A. Hutcheson

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Enclosure

cc: T. Osdene
E. Sanders
J. Seeman
C. Chavdarian

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